Complete Summary

GUIDELINE TITLE

Gonorrhoea. In: Sexually transmitted infections: UK national screening and testing guidelines.

BIBLIOGRAPHIC SOURCE(S)

Ison C, Jungmann E, Bignell C. Gonorrhoea. In: Ross J, Ison C, Carder C, Lewis D, Mercey D, Young H. Sexually transmitted infections: UK national screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); 2006 Aug. p. 16-25. [33 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Gonorrhea

GUIDELINE CATEGORY

Diagnosis
Evaluation
Risk Assessment
Screening

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Urology

INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To provide advice on what tests for gonorrhoea are most appropriate in a United Kingdom genitourinary (GU) clinic setting (excluding human immunodeficiency virus [HIV]-infected patients)
- To provide a basis for audit
- To support clinics when bidding for additional resources to meet national standards

TARGET POPULATION

Individuals in the United Kingdom with or at risk for gonorrhea

INTERVENTIONS AND PRACTICES CONSIDERED

Tests

1. Microscopy for intracellular Gram-negative diplococci
2. Isolation of *Neisseria gonorrhoeae*
3. Nucleic acid hybridization or amplification tests (NAATs)

Sites for Testing

1. Sampling by loop or cotton-tipped swab culture of mucosal sites, as appropriate, including endocervix, urethra, rectum, oropharynx, urine, vagina, Bartholin's duct, and ophthalmic and systemic sites
2. Special considerations for screening of heterosexual women, heterosexual men, men who have sex with men, women who have had a hysterectomy, 'young' men and women, pregnancy, sex workers, victims of sexual assault, and sexual contacts of individuals with gonococcal infection
3. Patient assessment after treatment, including test of cure when appropriate

MAJOR OUTCOMES CONSIDERED

- Test sensitivity and specificity
- Test positive predictive value (PPV)

- Accuracy of diagnosis

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

This guideline was obtained by searching the PubMed database 1970 to October 2004 using the terms gonorrhoea and diagnosis. All entries in English language were considered. The 2005 National guideline on the management of gonorrhoea in adults, the European guideline for the management of gonorrhoea and the Centers for Disease Control & Prevention recommendations for screening tests to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections - 2002 were also consulted.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well designed quasi-experimental study

III: Evidence obtained from well designed non-experimental descriptive studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guidelines have been developed following the methodological framework of the Appraisal of Guidelines Research and Evaluation instrument (AGREE - adapted as described in *Int J STD and AIDS* 2004 15:297-305).

The extent to which the guideline represents the views of intended users has been addressed primarily by the authorship coming from the multidisciplinary membership of the Bacterial Special Interest Group (BSIG). As practising clinicians the authors were able to draw on their experience of applying the tests to symptomatic and asymptomatic patients, but it was not feasible to obtain formal input from representative patients.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

A. Evidence at level Ia or Ib
B. Evidence at level IIa, IIb, III
C. Evidence at level IV

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After drafting the original guideline document, other health care professionals and professional bodies in genitourinary (GU) medicine were asked to comment, the draft guidelines posted on the British Association for Sexual Health and HIV (BASHH) website for 3 months, and all comments reviewed before final publication.

The guideline was edited by the Clinical Effectiveness Group of BASHH.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the level of evidence (**I-IV**) and grade of recommendation (**A-C**) are provided at the end of the "Major Recommendations" field.

Tests

Microscopy for Intracellular Gram-Negative Diplococci

Microscopical examination of Gram-stained smears of urethral discharge in men or endocervical discharge can be used as a near patient test to provide an immediate presumptive diagnosis of gonorrhoea (**Evidence Level II**, **Grade of Recommendation B**). In men, microscopy of urethral smears has a sensitivity of >95% in symptomatic patients, lower in asymptomatic patients (50% to 75%). Microscopy of endocervical smears in women has a sensitivity of between 30% to 50%. Specificity is high when screened by trained personnel, >99%. Microscopy is not suitable for pharyngeal or rectal specimens where many other bacteria are present including Gram negative cocci belonging to other genera.

Isolation of *Neisseria Gonorrhoeae*

- Specimens collected from an appropriate site should be cultured onto an enriched medium, usually GC agar base or Columbia agar, supplemented with lysed or chocolatised horse blood or a non-blood based supplement such as IsoVitaleX (Becton-Dickinson) or Vitox (Oxoid) (**Evidence Level II**, **Grade of Recommendation B**). If a single medium is used this should contain antimicrobial agents as selective agents to suppress the normal flora and allow the growth of *N. gonorrhoeae* (GC audit) (**Evidence Level II**, **Grade of Recommendation B**). Antibiotic cocktails, available commercially, contain vancomycin or lincomycin (to inhibit Gram positive organisms), colistin and trimethoprim (to inhibit other Gram negative organisms) and nystatin or amphotericin (to inhibit *Candida spp*.). Lincomycin is sometimes preferred over vancomycin because Env mutants with increased susceptibility to vancomycin do not grow. However, lincomycin is less inhibitory than vancomycin and overgrowth of normal flora can occur particularly with rectal or pharyngeal specimens. Trimethoprim sensitive strains can also occur. Choice of selective agents is dependent on the sites being screened. If resources are available culture on a non-selective medium in addition is ideal (**Grade of Recommendation C**). The primary isolation medium should be incubated in a carbon dioxide (CO_2) enriched environment for 48 hours before discarded as negative.
- Direct plating of the specimen and use of transport swabs both give acceptable results (**Evidence Level IV**). Culture plates inoculated directly should be kept at 37 degrees C, in the presence of 5% to 7% carbon dioxide if possible, before and after transfer to the laboratory. Transport swabs should be stored in the refrigerator at +4 degrees C and transported to the laboratory as soon as possible, preferably within 48 hours (**Evidence Level IV**).

- All colonies isolated on specialised media for *Neisseria* that are oxidase positive Gram negative cocci should be further identified using biochemical or immunological tests (**Grade of Recommendation C**). With confirmation, culture has a specificity of 100% and positive predictive value (PPV) of 100%.
- Culture for *N. gonorrhoeae* can be used with specimens from all sites and provides a viable organism for antimicrobial susceptibility testing. Culture has been reported to have a sensitivity for urethral and endocervical infection between 85% to 95% where conditions for culture are optimal. However, in settings where optimisation of culture is difficult the sensitivity of culture may be lower, particularly in comparison to nucleic amplification methods. Methods for confirmation of *N. gonorrhoeae* vary greatly.

Nucleic Acid Hybridisation or Amplification Tests (NAATs)

- Tests that probe or amplify specific nucleic acid sequences have the ability to detect small amounts of nucleic acid and can detect non-viable organisms. These tests can be used with non-invasive samples such as urine or self-taken swabs. Although NAATs offer high sensitivity (95%) for endocervical and urethral samples they are currently not recommended for screening in genitourinary (GU) Medicine clinics where samples are directly taken from mucosal surfaces because they do not provide a viable organism for susceptibility testing and PPV is <100% (**Grade of Recommendation C**). No molecular test to detect all known mechanisms of antibiotic resistance currently exists.
- The nucleic acid hybridisation test available is Gen-Probe, Pace 2 and Pace 2C, which has a sensitivity comparable to culture estimated to be 92.1% for endocervical and 96.4% for urethral specimens. The specificity of Pace 2 appears to be 99% using discrepant analysis.
- Three nucleic acid amplification tests (NAATs) are commercially available, COBAS AMPLICOR (Roche), BD ProbeTec-SDA (Becton Dickinsen) and Gen-Probe APTIMA Combo 2 (Biomerieux). The sensitivity of these tests is high (>90%) in comparison to culture (50% to 60%) for all specimens (endocervical swabs, self taken vaginal swabs, tampons, urethral swabs and male urines), except for female urines, where the sensitivity has been found to be lower (30% to 60%). The absolute values in the comparison of the sensitivities, between NAATs and culture, differ between studies and reflect inconsistencies in the definition used for a true positive and differences in collection and transport of specimens which may reduce the sensitivity of culture.
- All positive nucleic acid tests should be considered presumptive evidence of infection within a GU Medicine clinic setting. Where the prevalence of gonorrhoea is low, PPV may be <80% and culture confirmation of a positive NAAT result is recommended (**Grade of Recommendation C**).
- Nucleic acid tests have had limited evaluation on rectal and oropharyngeal samples but may have increased sensitivity (>90%) compared to cultures (<60%) taken from these sites. They are not currently licensed or recommended for testing at these sites (**Grade of Recommendation C**).

Recommendation

Factors determining the choice of screening test for *Neisseria gonorrhoeae* include test sensitivity, ability to assess antimicrobial susceptibility, ease of specimen

collection, cost, biological site tested, tolerance of possible non-culture false positive results, specimen transport and laboratory capability. Within genitourinary medicine clinics, culture remains the preferred test for routine use on invasively collected samples (**Grade of Recommendation C**). NAATs are the recommended tests for urine and non-invasively collected samples (**Evidence Level II**, **Grade of Recommendation B**). The use of NAATs on endocervical and urethral specimens may offer advantages in terms of sensitivity and specimen transport but denies the opportunity for continuing surveillance of antimicrobial resistance.

Sites for Testing

- All mucosal sites associated with symptoms (discharge and/or pain) should be tested for *Neisseria gonorrhoeae* (**Grade of Recommendation C**).
- There is little evidence to guide testing protocols with respect to which sites to test when screening asymptomatic individuals. In women, the sensitivity of a single endocervical culture is 85% to 95% in detecting infection with *N. gonorrhoeae*. The urethra is the only site of infection in 6% of infected women. There has been no recent evaluation of the additional contribution of routinely taking rectal and pharyngeal specimens when screening women, although these sites should be sampled when there is a history of direct exposure (**Grade of Recommendation C**).
- Microscopy of Gram-stained endocervical and urethral smears has low (40% to 60%) sensitivity in screening asymptomatic patients. It is time-consuming and has considerable resource implications for a clinic. It is relevant in patients with symptoms or signs and when screening high-risk individuals who are unlikely to reattend for follow-up. Its routine utility in screening asymptomatic individuals warrants further evaluation.
- Samples may be taken by loop or cotton-tipped swab for culture. Samples for nucleic acid tests should be taken and transported as specified by the manufacturer of the test used.

Endocervix

Samples taken from the endocervix during speculum examination are suitable for microscopy, culture and nucleic acid tests. Vaginal lubricants should be avoided since some gels are toxic to *Neisseria gonorrhoeae* (**Evidence Level II**, **Grade of Recommendation B**).

Urethra

Samples directly taken from the urethra are suitable for microscopy, culture and nucleic acid tests. As with microscopy, NAATs are less sensitive using urethral specimens in men with asymptomatic infection than with symptomatic infection. For sampling, a loop or cotton-tipped swab is introduced 1 to 2 cm into the urethral orifice. A higher sensitivity for microscopy is reported for urethral samples taken with a plastic loop compared to those taken with a cotton-tipped swab (**Evidence Level III**).

Rectum

Rectal samples are suitable for culture (sensitivity not well-defined). However, the sensitivity of microscopy is low because of the large numbers of other bacteria present in the rectum and is not recommended on anorectal swabs (**Grade of Recommendation C**), although may be useful if smears are obtained following insertion of a proctoscope on symptomatic patients (**Evidence Level III**, **Grade of Recommendation C**). Nucleic acid tests are susceptible to false positive reactions due to contamination/cross-reaction and are not well evaluated at this site. Anorectal samples from patients without symptoms may be obtained by blindly passing a moist swab 2 to 4 cm into the anal canal, using lateral pressure to try and avoid any faecal mass (**Evidence Level III**, **Grade of Recommendation B**). Swabs with heavy faecal contamination should be discarded. In symptomatic patients, anorectal specimens should be obtained under direct vision following insertion of a proctoscope.

Oropharynx

Pharyngeal samples are suitable for culture (although sensitivity not defined). Nucleic acid tests are not well evaluated at this site and cross-reactions with other species are possible. Specimens are obtained wiping a swab over the posterior pharynx, tonsils and tonsillar crypts.

Urine

The first 15 to 30 ml of urine is collected after the patient has held urine for at least an hour. Urine samples should be tested using a NAAT. The sensitivity of testing urine using a NAAT to identify gonococcal infection in women is lower than testing an endocervical specimen. (**Evidence Level III**).

Vagina

Patient taken vaginal swabs or tampon specimens from the vagina are suitable for testing using a NAAT. Such samples offer a sensitive alternative for screening women who decline speculum examination or would be deterred from screening by the need for such an examination (**Evidence Level III**).

Neisseria gonorrhoeae may infect the vaginal mucosa of prepubertal girls. Vaginal samples should be cultured in these circumstances in view of the implications of the diagnosis and to provide diagnostic certainty (**Grade of Recommendation C**).

Bartholin's Duct

When a Bartholin's abscess is present, purulent material expressed from the duct may be cultured and stained for microscopy.

Ophthalmic and Systemic Sites

Ophthalmic samples are suitable for culture. Conjunctival samples are obtained by wiping a swab over the inner lower eye lid. All patients must be referred to an ophthalmologist (**Grade of Recommendation C**).

Proving infection in patients with suspected disseminated infection is sometimes difficult. Culture of blood and joint aspirate may confirm the diagnosis. Genital and pharyngeal samples should also be taken and have a higher yield in identifying the presence of *N. gonorrhoeae* (**Evidence Level III**).

Screening in Specific Patient Groups

Infection of mucosal surfaces with *Neisseria gonorrhoeae* may be, and often is, asymptomatic. Screening procedures/protocols are influenced by sexual history. A wider number of sites may need to be tested in symptomatic compared with asymptomatic individuals to include the symptomatic sites. A history of condom use for intercourse is generally not an indication to omit screening for gonorrhoea.

- **Heterosexual Women**

  A single endocervical test (culture) will detect 85% to 95% of women infected with *N. gonorrhoeae*. The urethra is the sole site of infection in 6% of infected women. There is no contemporary data on how frequently the rectum and/or pharynx are the sole site of infection; historically this has been low. Repeat testing gives a small increase in the diagnostic yield in women. An endocervical test (culture or nucleic acid) should be regarded as a core screening test for *Neisseria gonorrhoeae* in asymptomatic women receiving a speculum examination in GU Medicine clinics (**Grade of Recommendation C**). A urethral culture may be combined with a cervical culture on the same plate where direct plating is practised to increase sensitivity. Testing non-invasively collected samples (urine and vaginal or vulval samples) should currently be reserved for women not undergoing speculum examination (**Grade of Recommendation C**). Non-invasive samples should be tested by a NAAT. Rectal and pharyngeal tests should be taken when directed by sexual history or symptoms (**Grade of Recommendation C**).

- **Heterosexual Men**

  Urethral swab or first catch urine test. Microscopy of a urethral smear may allow immediate presumptive diagnosis, but all men should receive a sensitive direct identification test (**Grade of Recommendation C**).

- **Men Who Have Sex with Men**

  Tests should be taken from all sites (urethra, rectum and oropharynx) potentially exposed to infection as directed by the sexual history (**Grade of Recommendation C**). Rectal infection may be acquired by transmission from the oropharynx in the absence of penetrative anal intercourse.

- **Women Who Have Had a Hysterectomy**

  Urethral swab for culture offers a better yield than high vaginal culture.

- **'Young' Men and Women**

Testing in post-pubertal young men and women follows that in adults. Young people may be intimidated by the prospect of invasive tests and may prefer non-invasive options when available, notably urine testing.

- **Pregnancy**

  Screening tests as for heterosexual women.

- **Sex Workers**

  Test all sites potentially exposed to infection as indicated by sexually history. Testing should generally proceed at sites apparently protected by consistent condom use (**Grade of Recommendation C**).

- **Sexual Assault**

  Culture is the recommended method for detecting *Neisseria gonorrhoeae* at all sites following sexual assault in adults because of 100% specificity (**Grade of Recommendation C**). Tests should include all sites potentially exposed to infection.

- **Sexual Contacts of Individuals with Gonococcal Infection**

  Consider including rectal test in addition to endocervical and urethral tests in female contacts (**Grade of Recommendation C**). Consider pharyngeal test in cases of oropharyngeal contact.

Test of Cure

Patients should be assessed after treatment. A test of cure is not routinely necessary when infection has been treated with a recommended directly observed therapy, symptoms have resolved and there is no risk of reinfection. If the patient is symptomatic, received a suboptimal treatment, a potentially resistant strain is identified on culture or there is a possibility of reinfection, test of cure with culture is advised. Pregnancy does not impair treatment efficacy. Efficacy of treatment at eradicating pharyngeal infection is lower for some antimicrobials than their efficacy at ano-genital sites. Test of cure is recommended following treatment for pharyngeal infection (**Grade of Recommendation C**).

Frequency of Screening in Asymptomatic Patients

Advice on frequency of screening in the absence of symptoms is dependent on individual risk for infection and is determined by pragmatism rather than prospective studies. Young people with a history of gonorrhoea may be at higher risk of repeat infection; encouragement for repeat screening may be prudent although screening intervals have not been defined.

Definitions:

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well designed quasi-experimental study

III: Evidence obtained from well designed non-experimental descriptive studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grading of Recommendations

A. Evidence at level Ia or Ib
B. Evidence at level IIa, IIb, III
C. Evidence at level IV

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accurate diagnosis of gonorrhea

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Ison C, Jungmann E, Bignell C. Gonorrhoea. In: Ross J, Ison C, Carder C, Lewis D, Mercey D, Young H. Sexually transmitted infections: UK national screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); 2006 Aug. p. 16-25. [33 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Aug

GUIDELINE DEVELOPER(S)

British Association for Sexual Health and HIV - Medical Specialty Society

SOURCE(S) OF FUNDING

No specific or external funding was sought or provided in the development of this guideline.

GUIDELINE COMMITTEE

Screening Guidelines Steering Committee
Clinical Effectiveness Group (CEG)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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Clinical Effectiveness Group (CEG) Members: Chairman Keith Radcliffe; Imtyaz Ahmed-Jushuf; David Daniels; Mark FitzGerald; Guy Rooney; Jan Welch

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The guideline was developed without patient or public involvement.

Conflict of Interest:

Catherine Ison: None
Eva Jungmann: None
Chris J. Bignell: None

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from British Association for Sexual Health and HIV Web Site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Specifications for the development of UK guidelines on the management of sexually transmitted infections (STIs) and closely related conditions 2005. London (UK): British Association of Sexual Health and HIV (BASHH); 2005. 14 p. Electronic copies: Available in Portable Document Format (PDF) from the British Association for Sexual Health and HIV Web site.

Additionally, auditable outcome measures can be found in the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on June 19, 2008. The information was verified by the guideline developer on October 20, 2008.

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